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CIRCULATORY ADJUSTMENTS TO PREGNANCY*†‡

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Research Professor of Clinical Medicine, Harvard Medical School

Received for publication May 19, 1954

It is a great honor to be asked to give a lecture named for Dr. William Sydney Thayer, the distinguished physician and teacher, and for his talented lady. For many reasons, some of them happily visible in this room, it is for me a special pleasure to have this generous opportunity, and I thank you for it.

On February 26, 1917 Dr. Thayer delivered a lecture in the Harvard Medical School, of which he was a distinguished graduate in the Class of 1889. The occasion of his lecture was the award of the John Harvard Scholarships; his title: "Scholarship in Medicine" (1). It is a wise and charming essay quite characteristic of its author.

As one who has given his share of general addresses, sometimes I have had my doubts about their utility, but I can testify that Dr. Thayer's scholarly enthusiasm for medicine made a deep and lasting impression on one second year medical student in the back row.

Two years after this experience I was delighted to find Dr. Thayer's name cut in the lid of an old slant-top desk in my room in the internes' quarters at the Massachusetts General Hospital. Beginning in 1921 it was my great privilege to see Dr. Thayer at close range and to come to regard him with admiration and affection during the happy years I spent at the Johns Hopkins Hospital in association with Dr. G. Canby Robinson.

William Sydney Thayer was a student of medicine. In the proud succession of Hippocrates and Sydenham, he sought to see and to understand the course and the evolution of disease. What Abraham Cowley wrote about William Harvey could properly be said of Dr. Thayer:

> "Thus Harvey sought for Truth in Truth's own Book,
> The Creatures, which by God himself was writ;
> and wisely thought 'twas fit,
> Not to read Comments only upon it,
> But on th' Original itself to look."

* Lecture I of the twentieth course of lectures under the William Sydney Thayer and Susan Read Thayer Lectureship in Clinical Medicine. Delivered at The Johns Hopkins Hospital, March 24, 1954.

† From the Department of Medicine of the Harvard Medical School and the Medical Services of the Boston Lying-in and Peter Bent Brigham Hospitals, Boston.

‡ Supported in part by the Higgins Fund through Harvard University and by a grant from the U. S. Public Health Service.

Dr. Thayer wished to understand the natural history of disease and the factors that influence its course. He would, I think, look with interest on the general subject matter of these two lectures, in which an attempt will be made to formulate some of the influences of pregnancy and disease upon each other. My knowledge of this field comes from two varieties of experience: first, studies of the physiology of pregnant women which have extended over the last twenty years and which have been expanded in the last three in a medical research laboratory located in the Boston Lying-in Hospital; second, a growing and current experience with the medical problems of pregnancy obtained on the active medical service which our obstetrical colleagues under the stimulating leadership of Dr. Duncan Reid have encouraged us to establish in the same Hospital. Both groups have the advantage of following in the path of a distinguished predecessor with great experience and with high standards, Dr. Burton Hamilton (2).

A general principle we endeavor to apply to the study and to the care of disease processes in pregnant women is as follows:

The physiological mechanisms of disease interact with the physiological mechanisms of pregnancy; to understand disease in pregnancy, it is necessary to define these two sets of mechanisms and to understand their interaction with one another. There is a wider objective also: from the observation of patients during pregnancy, facts about disease may be learned which can be applied to the non-pregnant.

The maternal organism provides the foetus with the environment and the nutrition required in his development. In doing this, profound changes occur in the maternal organs and tissues. A number of these involve the cardiovascular system. These lectures will be specifically concerned with the circulatory adjustments of the mother and their relation to her diseases. The physiological evolution and the ultimate victory of the growing foetus, however fascinating, are for the moment outside our subject.

We may begin by summarizing some of the available observations of what changes actually occur in the circulatory and some related systems of the mother during pregnancy. Some of these observations were made by the group at Vanderbilt in the early thirties (3), some by Dr. Eugene C. Eppinger in my laboratory at the Brigham during the early forties, and some in the course of recent work of the group at the Boston Lying-in Hospital. Many are taken from the excellent reports available in the literature. A few relatively modern concepts will be introduced, but the general nature of the circulatory adaptations to pregnancy has been obvious for many years. This is demonstrated by Dr. Angus MacDonald of Edinburgh in his book entitled "Bearings of Chronic Disease of the Heart upon Pregnancy, Parturition, and Childbed" (4) published in 1878. Dr. MacDonald, as we shall see, had pretty modern opinions, if not facts, about blood volume, cardiac output, and leg venous pressure

in pregnant women. Moreover, he reminds us that women with heart disease come to physicians asking for advice as to marriage and childbearing, and makes the following comment: "Now, though I believe that under such circumstances ladies will almost invariably ask their doctor's advice and follow their own liking, yet we ought to be able to give sound counsel." Both his wisdom and his physiological information are calculated to instill humility into the spirit of the present-day student.

We turn now to a consideration of some relevant adjustments to pregnancy in the mother's machinery.

OXYGEN CONSUMPTION

As one measure of the metabolic price of pregnancy, we may consider the oxygen absorption of the mother.

It is to be expected that the rapidly growing foetal tissues and the maternal organs that support them will require additional supplies of oxygen. Our measurements have indicated that there is an increase in oxygen consumption; that this rises progressively throughout pregnancy reaching its maximum in the last month; and that it amounts, in patients under scrupulous basal conditions, to a maximum about 20 per cent above the non-pregnant level.

It is more than an assumption that much of this oxygen is consumed by the foetal tissues and the maternal organs concerned with supporting them. Barcroft (5) has shown in several species of animals an oxygen consumption of about 5 to 7 cc. per minute per kilogram of uterus and contents. Recently Metcalfe, Romney, and their co-workers have modified the Kety method for local blood flow (6) and applied it to the measurement of the uterine blood flow in women during caesarean section performed at term. When this measurement is combined with determinations of the oxygen content of arterial blood and uterine venous blood, the data are at hand for calculating the oxygen consumption of the uterus and its contents.

The figures obtained by Dr. Metcalfe and his colleagues in our laboratory indicate that at term there is an oxygen consumption by the human uterus and its contents of about 5 to 7 cc. per kilogram per minute—a figure similar to that observed by Barcroft in animals. An adult body usually requires less than this volume of oxygen per kilogram, a fact which suggests that young and growing tissues have an active metabolism. The uterus and its contents account for about 70 to 80 per cent of the increased oxygen consumption of the maternal organism during pregnancy. The increased work of the maternal heart probably accounts for some of the remainder.

The maximum increase in the rate of oxygen consumption by the mother during pregnancy is not a great increase when compared with that associated with muscular work, but the increase of pregnancy is present day and night, at rest as well as during activity. The figures presented measure only the

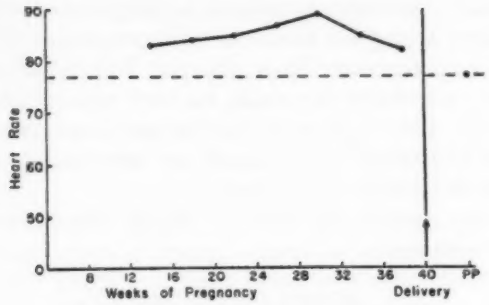

FIG. 1. Heart rate during pregnancy.

total *oxygen* consumption. A more direct estimate of the burden of pregnancy on the heart may be obtained by measurements of the maternal circulation itself.

Two general points should be made in advance about the circulatory adjustments in pregnancy: first, the curves presented represent *average* figures and variation between individual patients is wide; second, adaptations easily borne by a healthy woman may impose a troubling or even insuperable load upon an unhealthy one.

HEART RATE

Consideration will first be given to changes in the heart rate. Observations reported in Figure 1 represent the average changes in the basal heart rate of six women who were observed repeatedly throughout pregnancy and in the puerperium.

Scrupulous attention was paid to the maintenance of so-called basal or standard conditions and each point represents the average of many counts. It is apparent that there is a rise in heart rate early in pregnancy; that this rise attains a maximum about the eighth month; and that the rate is somewhat lower in the last weeks of pregnancy than at this maximum. After delivery has been accomplished, the rate returns to one which resembles the average for non-pregnant women. The increase in the latter part of pregnancy amounts to about ten beats per minute. This may seem trifling, but it means upwards of 14,000 extra heart beats per day.

BLOOD PRESSURE

Figure 2 sets forth serial observations on the systolic and diastolic blood pressure of pregnant women. It is observed that in these women studied under these conditions there is no significant change in the systolic pressure and a slight fall in the diastolic pressure. The maximum *pulse pressure* is

attained in the eighth month at about the same time as the maximum pulse rate. The observations of Werkö (7) indicate that in the pulmonary artery the pressures are normal in early pregnancy and may be slightly lower than normal during the last trimester.

OUTPUT OF THE HEART

The output of the heart is so closely related to the work of the heart that its measurement is particularly important in this discussion. Figure 3 portrays two curves. The lower one represents multiple studies of cardiac output made throughout pregnancy and in the puerperium by the acetylene method charted as the average for each month. Six women were studied in this way: four at Vanderbilt and two at Harvard. It is seen that the measured cardiac output

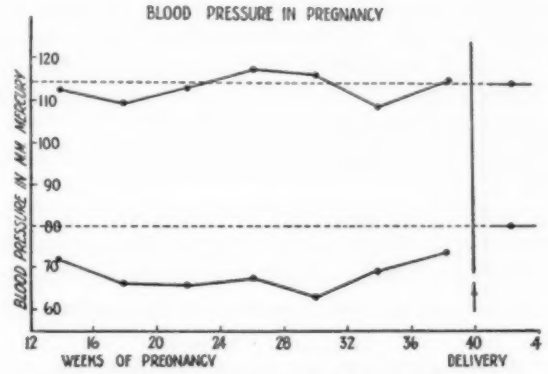

FIG. 2. Arterial blood pressure during pregnancy.

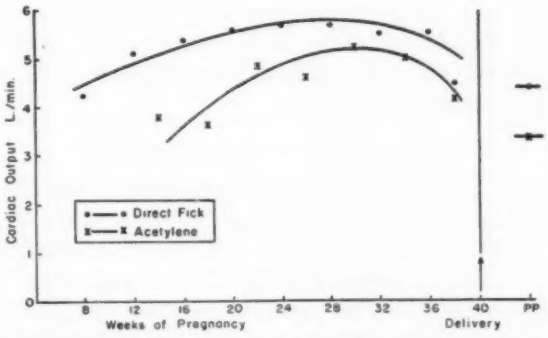

FIG. 3. Cardiac output during pregnancy (The "direct Fick" curve is drawn from the figures published by Hamilton (8)).

rises to a maximum at about the eighth month and that it is lower in the last month than at its maximum, but still above the postpartum or normal figure.

The upper curve represents the figures obtained by Dr. Hilary Hamilton in Professor Kellar's Department of Obstetrics in the University of Edinburgh (8). These figures were obtained by the direct Fick method during cardiac catheterization and were necessarily single observations at various stages of pregnancy in a larger number of women. They are also charted as the average for each month. The curve is the same shape as the one obtained by the acetylene method; the maximum flow occurs at a similar time and there is a fall in the last weeks of pregnancy. It is higher in all parts of the curve than the acetylene figures, but this relation between flows by the direct Fick method and the acetylene method is well established. The direct Fick results are then in general conformity with the findings by the acetylene method.

The total evidence makes it quite clear that pregnancy is associated with an increased output of the heart at rest. The work of Schmidt (9) suggests further that a given degree of muscular exercise leads to a greater increase in cardiac output during pregnancy than afterwards.

The following points in relation to the cardiac output of pregnant women are emphasized:

First, the increase during pregnancy is considerable and at its maximum usually amounts to 40 or 50 per cent or more over the non-pregnant level.

Second, the increase in cardiac output due to pregnancy is present twenty-four hours a day and is not discontinuous like the cardiac output increase due to exercise.

Third, the cardiac output does not increase in direct proportion to foetal weight, or to the total oxygen consumption of the mother; it increases out of proportion to both.

Fourth, in the last weeks of pregnancy the cardiac output is lower than at its maximum. This fall has taken place in each woman studied. Whatever the mechanism of this fall, it functions as a useful preparation for the circulatory stresses of parturition.

DISTRIBUTION OF CARDIAC OUTPUT

The distribution of the increased cardiac output is now to be considered.

Observations have been made by Munnell and Taylor (10) on the blood flow through the liver of pregnant women; by McCall (11) on the blood flow through the brain; and by Welsh, Wellen, and Taylor (12) on the blood flow through the kidney. In general, during the period of increased cardiac output in pregnant women, there is neither increase nor decrease in the blood flow through the liver, the brain, or the kidney. The blood flow in the peripheral parts of the maternal body has been studied by Abramson, Flachs, and Fierst (13) and

TABLE I
Uterine Blood Flow and Oxygen Consumption

WT. OF BABY	UTERINE BLOOD FLOW	UTERINE $\dot{Q}_{O_2}$	$\dot{Q}_{O_2}$/Kg. BABY
Kg.	*cc/min.*	*cc/min.*	
4.1	585	17.5	4.1
3.6	530	17.8	4.9
3.8	560	21.0	5.4
3.6	480	15.6	4.3
4.2	480	29.0	6.8
3.4	255	13.0	3.8
8.3	1185	49.7	6.0
4.4	582	23.3	5.3 Average

by Burt (14). The metabolically active foetus must lose heat to the mother, and this heat in turn must be eliminated. In this connection, both Abramson *et al.* and Burt have reported a substantial increase in blood flow through the *hands* of pregnant women. It is a frequent observation in pregnancy that the palms are reddened and may suggest the skin color observed in these areas in patients with hepatic disease. Whatever its mechanism, increased blood flow through the hands can play a useful role in favoring the elimination of heat. The idea of a change in the hand circulation during pregnancy is not new. In 1862, according to Burt, Raynaud recorded that one of his patients was accustomed to diagnose her own pregnancy by her freedom from vasospastic attacks.

UTERINE BLOOD FLOW

The main recipient of the increased cardiac output is the pregnant uterus and its contents. Measurements of the volume of uterine blood flow have been made by Metcalfe, Romney, and their co-workers (6). (Because of modifications in the method, these figures are quite different from those published by Assali and his co-workers (15, 15a). Table I reports the results of Metcalfe and his colleagues in seven women with single pregnancies and in one with twins. The results are in general conformity. The uterine blood flow per minute is of the general magnitude of 0.5 liters in the patients with one foetus, or about the same as the flow through one normal adult kidney. In the patient with twin pregnancy, the figure is approximately doubled.

It is necessary for foetal growth that a considerable volume of blood traverse the placenta. Here there is an arrangement by which the foetal blood is brought into close relation with maternal blood. The larger the flow through the placenta the higher will be the oxygen tension in the umbilical veins; the lower the placental flow, the greater the degree of anoxia under which the foetus must live and develop. There is thus a conflict of interests. A large placental

flow is good for the oxygen tension of the baby and demands increased work by the mother's heart. We observe, in fact, a biological compromise between foetal and maternal concerns.

The factors which control the volume of placental flow have not been clearly established. The combination of a large volume of flow and a relatively high pressure in the uterine veins suggest that the placenta is an area of low resistance. Data are not yet in hand to permit a calculation of this resistance. In the placenta the maternal blood pours from arteries larger than arterioles into the intervillous space, thence flowing into the veins. Thus it has some, but certainly not all, of the characteristics of an arteriovenous fistula, and this is one of several factors that modify the maternal circulation.

Of course the volume of placental blood flow is by no means the only factor in the adequacy of oxygen supply to the foetus. There is a series of elegant adaptations which improve the situation of the foetus with regard to oxygen. These include a special variety of hemoglobin, a considerable foetal polycythemia, and a thrifty arrangement by which relatively well oxygenated blood is distributed to the foetal tissues most susceptible to oxygen lack.

The volume of blood flowing into the intervillous space is apparently supplied without depriving any maternal organ or tissue of its customary supply of blood. Here again the demands of pregnancy are found to be different from the demands of exercise which may temporarily deflect blood from flow through essential organs to flow through somatic muscles. The adjustment to pregnancy by increasing cardiac output is sufficiently generous so that the output increases more than the oxygen consumption. This means of course that the maternal arteriovenous difference is diminished—that is, that the mixed venous blood in the right heart of the mother contains a higher percentage of oxygen saturation when she is pregnant than when she is not pregnant. The factors which determine the degree of cardiac output increase in a given patient are not yet known.

BLOOD VOLUME

It was accepted by Dr. Angus MacDonald in 1878 that the total blood volume was increased in pregnant women. In recent years the blood volume in pregnancy has been measured by many methods both direct and indirect. The careful studies of Thomson, Hirsheimer, Gibson, and Evans (16) are illustrative of a general agreement that there is a rise during pregnancy in both the plasma volume and the red cell mass. The plasma volume increase is the greater so that the red cell and hemoglobin percentage values are lowered. Figure 4 is drawn from the data of Thomson, Hirsheimer, Gibson, and Evans. (16) The curve of total blood volume follows much the same course as that of cardiac output, reaching a maximum at about the eighth month and declining in the last weeks of pregnancy. The curve of red cell mass continues to rise un-

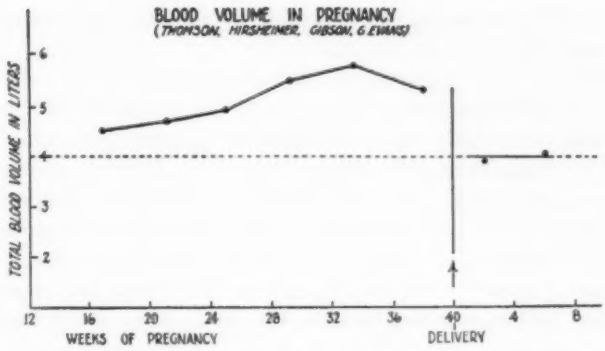

FIG. 4. Blood volume during pregnancy (drawn from the data of Thomson, Hirsheimer, Gibson, and Evans (16)).

til the end of pregnancy (16a). The curve of plasma volume drops strikingly in the last weeks in spite of the fact that total body water rises continuously till the end of pregnancy. This has been studied by Haley and Woodbury (17) in our laboratory, and by Hutchinson, Plentl, and Taylor (18) at Columbia by the method of heavy water dilution. Haley and Woodbury point out that during the last weeks of pregnancy there is a *selective* accumulation of body water in excess of solids in the apparently normal patients studied. Nevertheless, the plasma volume falls.

DISTRIBUTION OF BLOOD VOLUME

Evidence is not available which permits a precise description of where the increased blood volume is to be found. Certainly a substantial amount is in the placenta and the uterine vessels. There is suggestive evidence that some is trapped in the vessels of the legs. Dr. Angus MacDonald in 1878 in his classical description of the physiological alterations of the circulation in pregnancy referred to "exalted venous tension" in the legs. In recent years this pressure has been measured by several workers. In general, the arm pressure has been within normal non-pregnant limits; the leg pressure has tended to rise progressively throughout pregnancy and to reach its maximum at term. The magnitude of the rise is of the order of 10 to 15 cm. H_2O. It is probable that the position of the body is a factor in the leg venous pressure and in the volume of blood in the leg vessels. These measurements were made when the patient was recumbent.

X-rays of the lungs during pregnancy may show "increased vascular markings," and this observation with its hint of increased pulmonary blood volume raises the question of lung volumes and lung mobility in pregnant women. There is another reason to study these matters: dyspnea is not rare during

pregnancy. It may be increased in recumbency and may, as a symptom, suggest the possibility of cardiac disease.

The heart and lungs are part of the same system, both concerned with the absorption and transport of oxygen and the transport and excretion of carbon dioxide. The ventilatory phenomena of pregnancy have been studied extensively by Metcalfe and Woodbury (19) in our laboratory and by Gaensler and his co-workers (20, 21, 22) at the Boston City Hospital. Only a few points will be made here, which apply directly to the problem under discussion.

First, the ventilation per minute is elevated and this increase in volume of ventilation is greater than the increase in the oxygen consumption. This disproportion indicates that pregnant women hyperventilate during pregnancy.

Second, as Dr. MacDonald was aware in 1878, pregnancy in itself does not cause a decrease in vital capacity. Metcalfe and Woodbury (19) have shown that the inspiratory reserve is increased more than enough to compensate for the decrease in expiratory reserve, as is shown in Figure 5. The resulting increase in vital capacity occurs at the expense of the residual lung volume. That the vital capacity is maintained or increased during pregnancy is a useful observation; it means that reduction in this function observed during pregnancy is not to be explained by the pregnancy, but must be due to some other cause.

The lung in pregnant women is in a relatively expiratory position, i.e. relatively collapsed. Gaensler and his colleagues (20, 21, 22) have pointed out the similarities between pregnancy and pneumoperitoneum in their effects on the lung volume. Merriman (23), working at the Peter Bent Brigham Hospital, has described changes in the pattern of ventilation in obese patients which in some ways resemble those of pregnancy—namely a reduced expiratory reserve volume in the presence of a normal vital capacity. When the obese

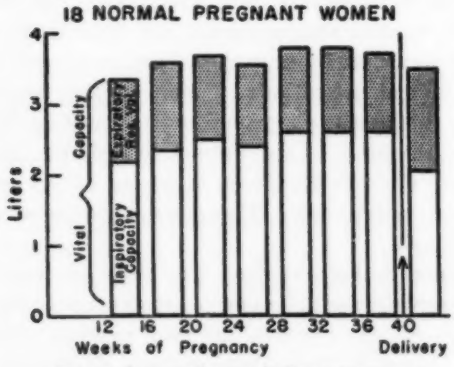

FIG. 5. Lung volumes during pregnancy.

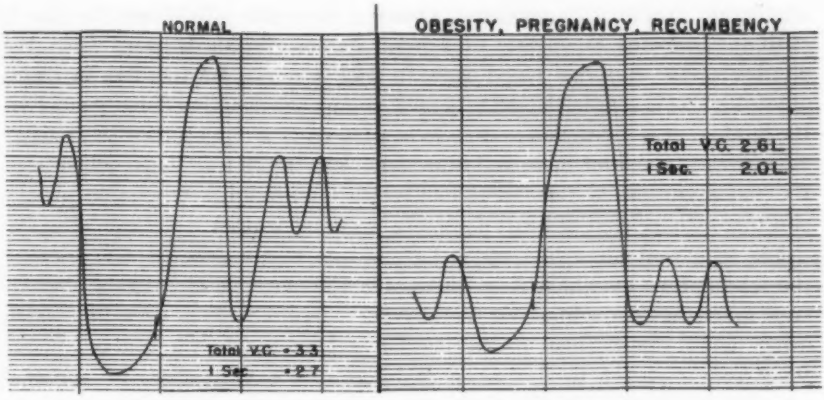

FIG. 6. Ventilation pattern influenced by obesity, pregnancy, and recumbency.

patient is in the supine position, the expiratory reserve volume falls still further.

When pregnancy and obesity co-exist, the reduction of expiratory reserve volume is still more marked. The patient whose ventilation is recorded in Figure 6 has a ventilation pattern modified by obesity, by pregnancy and by recumbency. She is obviously breathing in a position of almost complete expiration and with the lung at a degree of collapse when the resistance is high and air speed is slow. It is suggested that breathing with the lung thus deflated requires more effort and that this may be one factor in that unpleasant consciousness of labored breathing which we call the dyspnea of pregnancy.

These changes in the oxygen consumption, the heart rate, the arterial pressure, the cardiac output, the venous pressure, the blood volume, the ventilation and the lung volumes are some of the quantitative physiological alterations associated with pregnancy. These have been selected for description because knowledge of these can be applied directly to the management of heart disease in pregnant women. The degree of some of these changes in the maternal circulation differs in different women. One factor in this difference may be the number of foetuses in the uterus. In the observations on uterine blood flow and in our current studies of blood volume, there are strong suggestions that twins require greater adjustments on the part of the mother than do single pregnancies. At any rate, these adjustments in the maternal physiology have the general result of providing a suitable opportunity for the foetus to develop. It would be interesting to speculate on some of the quantitative relationships between these adjustments and the comfort and progress of the foetus. Is the volume of the uterine blood flow, as was suggested in an earlier paragraph, directly related to the oxygenation and nutrition of the foetus? Is the hyper-

ventilation exhibited by pregnant women a favorable adjustment in that it enables the foetus to operate at a lower carbon dioxide tension? Does the dilution of the maternal blood serve in itself some useful function in foetal physiology, is it simply the price of maintaining the effective blood volume of the mother, or is it truly an anemia to be prevented by appropriate treatment? To attempt to answer these and other questions would lead us far afield from the major purpose of this discussion, which is to build a foundation for the effective management of heart disease in pregnant women.

For somewhat different reasons I do not go into a detailed discussion of the mechanisms by which these changes in the maternal circulation of pregnant women are brought about. What is the complex chain of causation which brings about the changes in the plasma volume and in the red cell mass? What role is played by hormones, or by the mechanical effect of increased vascular capacity, or by the distribution of the blood volume. What sets the regulation of breathing at a higher level in relation to the oxygen consumption? These are questions the answers to which would bear directly on our problem. I do not discuss them because we have to date too little definitive and quantitative information.

Pregnancy itself is not the only problem for the maternal heart. There is another set of alterations in the circulation occurring during *labor*. Here again our information is far from complete, but two *examples* may be cited:

First, the oxygen consumption during labor has been studied by Sampson (24) and by others. The findings are in general agreement. It is evident that the oxygen consumption rises during labor and that the degree of increase is largely dependent upon the frequency of uterine contractions. The increase in oxygen consumption is discontinuous, i.e. there are intervening periods of uterine relaxation when the oxygen consumption is not increased. The *average* oxygen consumption per unit time in a labor of *average* rapidity indicates a total burden comparable to moderate muscular exercise. In labor with more frequent pains, it can be comparable to severe exercise.

Second, the heart rate during labor has been investigated in our Boston Lying-in Laboratory by Dr. Dorothy Twitchell. She studied this matter by continuous electrocardiographic recordings. Figure 7 indicates the type of alteration in heart rate which may take place during labor. To be noted are the following:

1. A rise in heart rate during the early seconds of a uterine contraction.
2. A marked slowing of the heart rate during that part of the uterine contraction in which, as Hamilton and his co-workers (25) have shown, the placental blood flow is sharply reduced.
3. A return to the resting level after the uterine contraction is over, emphasizing the discontinuous character of the work of labor.
4. Tachycardia during the time of actual delivery.

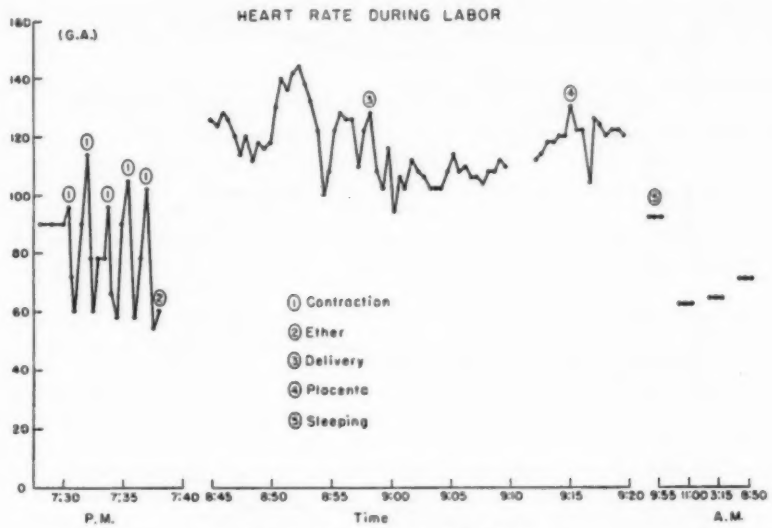

FIG. 7. Heart rate during labor.

5. An agreeable degree of postpartum bradycardia.

During parturition and the puerperium an intricate series of profound readjustments are being made. Adjustments *to* pregnancy are made gradually; some adjustments *from* pregnancy must take place suddenly. These adjustments include the re-establishment of normal water and electrolyte balance, a new equilibrium among the hormones and the tissues that produce them, and appropriate changes in the blood volume and the total capacity of the vascular system.

The observations referred to in this lecture have shown among the significant adaptations to pregnancy an increased oxygen consumption, an increased heart rate, an increased cardiac output, an increased blood volume, an increase in total body water, a rise in red cell mass, and an increase in venous pressure in the legs. These physiological adaptations to pregnancy are not static (after they are established) but follow a developing pattern. As the foetus grows, there is for about the first eight months or so a progressive rise in cardiac output, but in the last weeks of pregnancy, while the foetus continues to grow, the cardiac output diminishes and the heart rate falls. Blood volume also diminishes. At the same time the oxygen consumption, the red cell mass, the leg venous pressure, and the total body water are staying at a high level or even continuing to rise further. Thus we deal with a series of interlocking cycles rather than with simple or independent alterations in function.

Figure 8 illustrates this point. Here are charted the oxygen consumption, the heart rate, the cardiac output, and the total blood volume in one patient

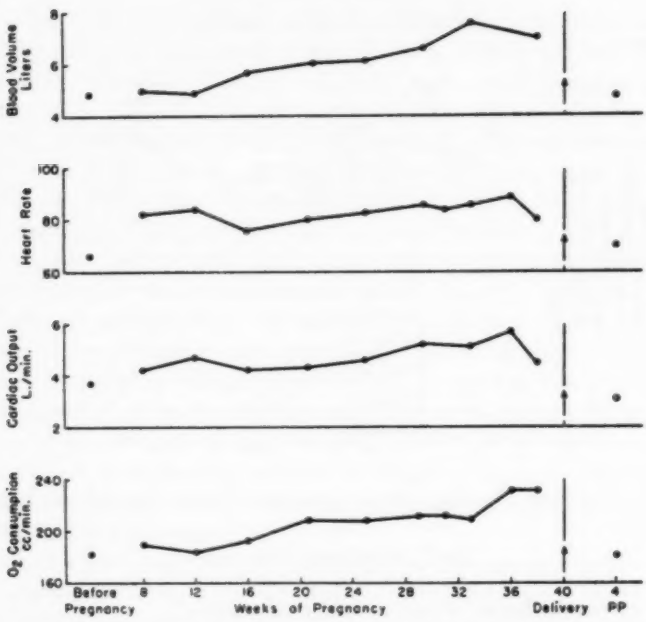

FIG. 8. Oxygen consumption, cardiac output, heart rate, and blood volume—before, during, and after pregnancy in the same patient.

studied repeatedly before, during, and after pregnancy. The changes in this individual follow the general pattern which has been described in this lecture, but the four functions do not vary directly with one another.

In summary, an attempt has been made to describe some of the modifications in circulation and respiration which are associated with pregnancy. In the next lecture we shall consider the application of these facts and concepts to the course and management of heart disease in pregnant women.

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THE MANAGEMENT OF HEART DISEASE IN PREGNANT WOMEN*†‡

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In this lecture an attempt will be made to apply the physiological observations described in the previous lecture to the management of pregnant women with heart disease. During the first three years of our experience at the Boston Lying-in Hospital we saw 201 women with heart disease through their pregnancies. These were not women with doubtful or so-called potential heart disease, or with only minor abnormalities of function. They were patients who exhibited one or more of the following evidences of heart disease.

1. *Obvious enlargement* of the heart by x-ray
2. *Congestive heart failure*
3. *Valve disease*
   - Mitral stenosis
   - Aortic insufficiency
   - Aortic stenosis
4. *Congenital deformity*
5. *Severe arrhythmia*
   - Auricular fibrillation
   - Auricular flutter
   - Complete heart block
6. *Angina pectoris*
7. *Pericarditis*, acute or chronic
8. *Bacterial endocarditis*
9. *Myocardial infarction or fibrosis*

Etiologically, these 201 examples of cardiac disease were divided as follows.

Rheumatic heart disease	178
Congenital heart disease	19
Hypertensive heart disease	3
Myocardial fibrosis—unknown etiology	1
	201

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Etiological distribution will obviously vary with climate, genetic composition of the population, and other variants, but it is apparent that in this clinic in Boston rheumatic heart disease is the major cardiac problem of pregnancy. An attempt was made to identify the predominant valvular lesion in each of the 178 women with rheumatic heart disease. Our recorded judgement, based on a discussion at a weekly history meeting, listed these as follows.

Mitral stenosis	125
Mitral insufficiency	39
Aortic insufficiency	8
Aortic stenosis	6

Since about two-thirds of these 201 patients had mitral stenosis as the chief mechanical problem, it will be appropriate to use mitral stenosis as an example of heart disease occurring with pregnancy. In this lecture we shall deal specifically with the interaction of pregnancy and mitral stenosis. The principles of management derived from this study of interaction can be applied also to the management of other types of heart disease.

Dexter and his colleagues have described the pathologic physiology of mitral stenosis (1). In summary terms, the mitral valve area is reduced in mitral stenosis and may be as low as $\frac{1}{10}$ its normal size. This reduced valve area imposes an obstruction to the circulation of the blood, and this obstruction is distal to the pulmonary capillaries.

As narrowing of the mitral valve progresses in the natural course of rheumatic valve disease, alterations in the circulation must occur. If cardiac output is maintained, the pressure in the left auricle must rise since the chief mechanism for accelerating the flow of blood through this narrow aperture is a rise of differential pressure. On the other hand, if left auricular pressure is maintained at the normal level, cardiac output must fall.

The human organism, with its great experience in meeting situations, handles this difficulty with a compromise. Both adjustments occur: the left auricular pressure rises; the cardiac output is somewhat reduced. A corollary of the pressure-flow relation is that in patients with mitral stenosis an *increase* in the volume of cardiac output per minute and hence in the flow through the mitral valve can in general be brought about only by a *further rise* in left auricular pressure.

Any rise in left auricular pressure is necessarily followed by a corresponding rise in pulmonary capillary pressure and may produce a related rise in pulmonary artery pressures.

A third change in the circulation should be mentioned which develops in some patients with severe mitral stenosis of long duration. This change is narrowing of the pulmonary arterioles. This creates another point of increased resistance and leads to further pulmonary artery hypertension, to additional work for the right ventricle, and to a further reduction in the cardiac output.

It is necessary to consider next the relation between *heart rate* and the blood flow through the mitral valve. Forward flow through this valve takes place only in diastole. In the normal person only a small part of the available diastolic time is needed for even large volumes of blood flow through the mitral valve. In the patient with severe mitral stenosis, on the other hand, much or all of the diastolic time is used for the flow of blood through the narrowed valve.

Figure 1, from calculations based on the formula of Lombard and Cope for the duration of systole (2), charts the relation between heart rate and total available diastolic time. It is seen that a rise in rate from 70 to 140 will cut the available diastolic time per minute by some nine seconds, or about 25 per cent. Such a reduction in available diastolic time, in patients with mitral stenosis, in itself may require a further increase in left auricular pressure in order to achieve a sufficiently rapid flow of blood through the narrow mitral valve to maintain the cardiac output. It is a matter of experience that patients with severe mitral stenosis may develop pulmonary edema within an hour or two of the onset of tachycardia.

Consider now the effects of pregnancy when superimposed on the already complex vascular dynamics of mitral stenosis. It has been shown that pregnancy is associated with a rise in cardiac output. There is evidence that this rise occurs in women with heart disease as well as in normal women. Schmidt (3) of Düsseldorf studied the cardiac output of five women with valvular heart disease before and after the interruption of pregnancy. The output was

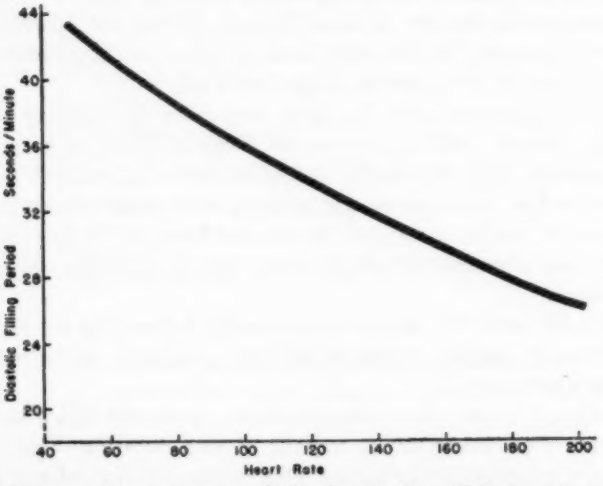

FIG. 1. Influence of heart rate on available diastolic time. (Calculated from the formula of Lombard and Cope (2)).

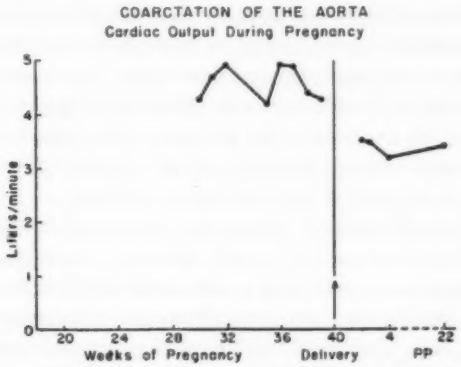

FIG. 2. Cardiac output during pregnancy in a patient with coarctation of the aorta.

greater during pregnancy. Strayhorn (4) studied the output of a women with coarctation of the aorta during the last trimester and after delivery. Figure 2 shows the increase he demonstrated during pregnancy.

The rise in cardiac output associated with pregnancy requires an increase in the rate of flow through the mitral valve. In a patient with mitral stenosis such an increase in rate of flow requires a rise in left auricular pressure. This leads in turn to an inescapable increase in pulmonary capillary pressure, and this places the pregnant woman with mitral stenosis closer to pulmonary edema than when she is not pregnant. The rise in left auricular and pulmonary capillary pressures is accentuated by any coincident rise in heart rate, whether this occurs from pregnancy or from other mechanisms. There is evidence that changes in the total blood volume may also affect these intravascular pressures. This will be true whether the changes in blood volume are due to pregnancy, to infusion or to sodium intake.

The principle of management in dealing with heart disease in pregnant women is, therefore, to adopt ways and means which limit or restrict the *cardiac output*, the *cardiac rate*, and the *total blood volume*. The physician must be concerned with the algebraic sum of factors influencing output, rate and volume; with the total cardiac load resulting from the patient's total situation, including pregnancy. To say it again, we attempt to make a place in the patient's cardiac budget for the expenditures of pregnancy by eliminating equivalent amounts of other expenditures. We turn, therefore, to a consideration of various factors which demand an increase in cardiac load and which have the further essential characteristic that they can be limited or eliminated. The objective is not necessarily to keep the total load at a minimum, but to keep it *safely within the individual patient's tolerance.*

Individual factors in patients' lives which lead to increase in heart rate, cardiac output, or blood volume include the following:

1. *Physical activity.* This is the most obvious and often the most important single factor. Probably a given degree of exercise demands more increase in cardiac output in a pregnant woman than when she is not pregnant. The physician deals with the limitation or prohibition of specific activities which his experience and his analysis of the patient's life suggest may be excessive for her. He deals with hours of work as well as intensity of work, and he deals equally carefully with hours of rest and hours of sleep.

2. *Emotional stress.* Emotional stress, by various mechanisms, can lead to increase in heart rate and cardiac output. Anxiety, for example, by affecting the patient's sleep pattern, may add to the total work burden for the twenty-four hour period. One has seen the precipitation of pulmonary edema by emotional stress. One of the emotional burdens of the pregnant cardiac is the necessity of her dealing with both the fact of pregnancy and the fact of heart disease. This may pose a special problem for the considerable group of women who learn for the first time during pregnancy that they have heart disease. The reassurance that the patient gains from confident optimism on the part of the physician may be an important factor. As Robinson wrote of heart disease (5) "... many of the patients illustrate how organic disease and emotional disturbance interact on one another to form a vicious circle". Education of the patient and her family may make a crucial difference between success and failure in negotiating pregnancy.

3. *Ectopic rhythms with tachycardia.* The sudden onset of paroxysmal tachycardia, or of auricular fibrillation or flutter with a rapid ventricular rate in patients with mitral stenosis, who have hitherto done well throughout pregnancy, may precipitate pulmonary edema rapidly. Szekely and Snaith (6) in Newcastle, have brought clear evidence of an increased tendency to attacks of paroxysmal auricular tachycardia during pregnancy. Normal rhythm is usually restored without difficulty, but prompt action may be necessary. In general, the usual methods of controlling rate and rhythm are effective in pregnant patients.

4. *Anemia.* It has been shown by numerous workers that a sufficient degree of anemia will call for increase in the cardiac output per minute (7). Most pregnant women undergo a dilution of their hemoglobin, and at the time of maximum dilution may have a hemoglobin lower by some 2 or 3 grams per 100 cc. than when in the non-pregnant state. In women with a normal amount of hemoglobin, such a degree of dilution does not bring about an anemia of the severity required to produce an increase in cardiac output, but if a patient starts her pregnancy with the hemoglobin level already low this may well fall to a point at which an increase in cardiac output is required.

Mrs. T. was a 25 year old woman who developed severe pulmonary edema following a transfusion in the sixth month of pregnancy. The pulmonary edema was so severe as to threaten her life. The chain of events when reconstructed

appears to be as follows: She had had mitral stenosis for some years. This was not severe and had never produced any limitation of activity or any suggestion of pulmonary edema. She was a member of a family most of whom had the Mediterranean anemia trait and she had been followed for years in a neighboring clinic which was able to tell us that her usual hemoglobin level was about ten grams. The onset of pregnancy was presumably followed by an increase in cardiac output due to the demands of pregnancy. As her cardiac output rose on the familiar pregnancy curve, another factor also entered the picture. Her hemoglobin underwent dilution by the characteristic disproportionate increase in her plasma volume. At the time of the transfusion her hemoglobin had fallen from its usual 10 grams to less than 7 grams per 100 cc., and her cardiac output was presumably increased by this influence as well as by her pregnancy. Her heart rate was demonstrably increased. By the time she entered the hospital she was badly frightened and this contributed further to her tachycardia. The immediate situation was met by such measures as morphia, temporary reduction of the blood volume with tourniquets, and physical inactivity. The long term situation was met by a series of small packed cell transfusions which over several days raised her hemoglobin to approximately 10 grams per 100 cc., without sudden increase in the blood volume. With this hemoglobin level her mitral valve was quite large enough to transmit the basic cardiac output plus the cardiac output required by pregnancy at left auricular pressures which did not lead to pulmonary edema.

5. *Obesity.* Many women gain weight generously during pregnancy. There is no good evidence that this increase in weight calls for an increased cardiac output at rest, but it does increase the oxygen requirement during exercise and hence means that exercise requires a larger cardiac output than if the weight were normal. Obesity also, as was pointed out in the previous lecture, has a contribution to make to the sensation of dyspnea.

6. *Infections.* It is a common experince of every doctor who observes patients with mitral stenosis over the years that they may have an increase in symptoms in association with acute infections. Here there are a number of factors which lead to an increase in cardiac load. They include fever and the physical work of coughing. Lobar pneumonia has been shown by Rutstein and his colleagues to be accompanied by an increase in total blood volume (8).

7. Hyperthyroidism, by leading to increased output and elevated heart rate, will impose a burden on the hearts of pregnant women with mitral stenosis.

8. Factors that influence the blood volume may influence the course of pregnant women with heart disease. Sudden increase, such as is brought about by infusions or transfusions, has been known to precipitate pulmonary edema. (9) This danger can be prevented by controlling the volume and rate of infusion or by avoiding them. Phlebotomy is a successful method of therapy in certain acute and threatening situations.

The physiological control of blood volume is not a simple matter, and is probably especially complex in pregnancy. Some factors which influence it can be identified and used. The regulation of sodium intake is an example. The exact effect of variations in ingested sodium on the blood volume of pregnant women is not known, but the following facts may apply. Lyons, Jacobson and Avery (10) demonstrated a significant increase in plasma volume after the ingestion of sodium chloride or bicarbonate in normal persons. Strauss (11) showed that the tendency of pregnant women to retain water may be diminished by restriction of sodium intake. We have observed that pregnant women on severe sodium restriction may develop postural hypotension and syncope of a type suggesting a reduction in the effective blood volume. These symptoms are relieved by increasing the salt intake. These facts combined with experience in the care of patients with heart disease emphasize the importance of adequate restriction of salt. Again and again we have seen a change in salt ration quite literally tip the scales.

Thus the first point in the management of heart disease in pregnant women has been the analysis of the *total* burden in each patient and the careful regulation of any controllable factors in this total load. It should be emphasized again that the *total load* imposed is one factor, the state of the patient's heart is the other. If the total load is great enough, congestive phenomena may be produced in patients with *minimal* heart disease, and we have seen one pregnant woman who after ingesting about a pound of sodium bicarbonate in about a week developed clear signs of pulmonary edema, although at no time were we able to demonstrate acceptable evidence of heart disease.

The second and related point is to make these adjustments with due consideration of the known variation in the burdens of pregnancy. We can exploit our knowledge of the curve of cardiac work in pregnancy; we can plan to exercise the most rigid control at the time of maximum load, and we can expect improvement in cardiac symptoms during the final weeks. Hamilton (12) pointed out many years ago that the incidence of congestive phenomena in pregnant patients with heart disease followed closely the curves of cardiac output and blood volume.

The chief method of managing these additive burdens is to give individual and informed attention to each patient. In our clinic they are cared for by close collaboration between obstetrician and medical man, the final responsibility being held of course by the obstetrician, the medical men acting as consultants and responsible advisers. Patients are followed during pregnancy in the out-patient medical clinic as well as in the pre-natal clinic. The medical clinic meets weekly and cardiacs are seen as often as once a week. With a medical resident and laboratory staff on duty all the time, there is a mechanism for meeting sudden developments without delay or confusion. Routine laboratory work is easily accessible in this out-patient clinic and special laboratory studies

can be done in the medical research laboratory when they are indicated. It has been found useful to have a technician on duty in the medical clinic to do a vital capacity at every visit of every cardiac patient. It is well known (as Dr. Angus MacDonald observed in 1878) (13) that pregnancy in itself does not reduce the vital capacity. Reduction in this measurement is therefore taken seriously, and has on several occasions been the sign that pointed to developing pulmonary congestion before symptoms or physical signs suggested it. In this medical clinic all the resources of a great obstetrical hospital are available and are used. Patients are admitted to the ward for study or treatment during pregnancy when necessary.

The 201 patients that were seen through pregnancy in the first three years of our new organization have, on the whole, done well. There has been one maternal death. This rate is obviously not statistically significant, but it is in general encouraging.

The third point in the general program is the control of specific disease processes which may directly injure the heart; for example: acute rheumatic fever or subacute bacterial endocarditis. It is better to prevent these than have to cure them. Fortunately, active rheumatic fever is not frequent during pregnancy, but it can certainly occur and may be dangerous. From time to time a patient will develop active rheumatic fever within a few days or weeks of delivery. One of our patients has done this after each of two deliveries. Rheumatic fever prophylaxis is advisable in such patients. Subacute bacterial endocarditis may occur during pregnancy or after delivery.

Transient bacteremia has been observed (14) at the time of delivery. The frequency of this under present-day conditions is not well documented. It appears still advisable to give antibiotics prophylactically to all women with rheumatic or congenital heart disease at the time of delivery. The frequency of bacteremia at parturition is now under study in our laboratory.

So far we have been discussing the conservative management of mitral stenosis occurring in conjunction with pregnancy. We consider now the radical solution of this problem by direct surgical attack first on the pregnancy, or second on the valve lesion.

Interruption of pregnancy is occasionally recommended as a means of preventing maternal mortality. There are patients who, early in pregnancy, develop failure which persists in spite of careful management, and in such instances, fortunately rare and getting rarer, termination of pregnancy may be necessary to save the mother's life. In the series here reported, interruption was carried out 21 times, or in 10 per cent of the patients, while 180 or 90 per cent of the patients went through their pregnancy. Ten of these interruptions were done in the first year. Increasing confidence in the ability of women with mitral stenosis to negotiate pregnancy, and improvement in the methods of dealing with heart disease in pregnant women have combined to lower this

incidence decisively. In the six months from July 1, 1953 to January 1, 1954, *no* interruptions were performed because of heart disease. Our present policy is to take the position that all women with heart disease can go through pregnancy and to hold this position until persistent disability under the best obtainable regimen has convinced us of the contrary. If pregnancy is to be terminated, it is of the greatest importance that this be done early (in general before the end of the fourth month) so that the procedure itself may be of minimum danger. If a hysterotomy is to be performed in a cardiac patient with failure, it is vital that the failure be treated first and she be in the best attainable condition at the time of operation.

Finally, we consider the role, if any, that the surgical treatment of mitral stenosis can play in the management of heart disease during pregnancy (15). Mitral stenosis is the main cardiac problem in pregnant women. The trouble with people with mitral stenosis is that the valve opening is too small. Appropriate surgical procedure can enlarge this opening. Therefore, it is necessary to consider the possibility that mitral surgery may be a useful method in the management of pregnant women with heart disease. It is of course early in the developing history of mitral valve surgery. Policies must be tentative and must be developed with due consideration of the special problems presented by pregnant patients. Our experience to date has led me to certain tentative conclusions. These are *my* conclusions and should not be taken as representing those of anyone else. They are as follows:

1. Women with mitral stenosis and pregnancy on the whole do well with informed medical treatment.

2. In many instances pregnant women with mitral stenosis can undergo an operation on the mitral valve and continue the pregnancy to a successful conclusion. Most of these women would probably do well without an operation if the medical supervision were adequate.

3. The total situation in pregnancy is more complicated than when the same patient is non-pregnant, and therefore the operation can be expected to carry a higher hazard.

4. There may be reactivation of rheumatic fever after mitral valve surgery.

5. The history of mitral surgery over recent years has shown that it is not always possible to evaluate the degree and importance of mitral stenosis preoperatively. *In any hands the diagnosis may be wrong.* We have seen two patients subjected to valvuloplasty during pregnancy in whom the extent of mitral regurgitation had been underestimated. When regurgitation turned out to be the main problem, these pregnant women had been subjected to a formidable operative procedure without improvement in cardiac function. Both required termination of pregnancy later; one survived after a long illness; one died.

Therefore, it is my opinion that mitral valve surgery during pregnancy should be recommended only in rare and special cases. These will be individuals

who have important and stubborn congestive phenomena in their pregnancy or who did badly in previous pregnancies. They will be patients in whom it can be shown that ideal medical management is not effective, and in my opinion they should be patients in whom the safer procedure of interruption is not practicable.

In my judgment, then, operation on the valve during pregnancy is usually *not* the best way to handle the problem of mitral stenosis. But I believe that there is a relation between pregnancy and mitral surgery more important than operation during pregnancy. A medical clinic in an obstetrical unit can be an effective case-finding agency. About half of our patients with rheumatic heart disease are not aware of its existence until they are studied in the medical clinic. The effectiveness in case-finding of such a clinic is partly due to the effect of pregnancy in making more obvious signs of heart disease. Murmurs that are impressive during pregnancy may become minimal or even disappear after delivery. Two conclusions follow. 1) Pregnancy helps diagnose the fact of the existence of heart disease. 2) The appraisal of the severity of mitral stenosis or other valvular disorder and a decision about the need of surgery is best made when pregnancy is completed, and the patient has been observed in the non-pregnant state. On the double basis of observation during pregnancy and reappraisal postpartum, a considerable group of our patients with mitral stenosis have undergone valvuloplasty after successfully completing pregnancy. They have done well. Several women whose pregnancies were interrupted because of mitral stenosis have been referred for surgery afterwards and had good results. A small number have gone through a subsequent pregnancy, obviously better able to deal with it than before operation. This, in my opinion, is the best way to use mitral surgery in relation to pregnancy. These results are so good that *mitral stenosis requiring the interruption of pregnancy is no longer necessarily an indication for sterilization.*

I do not wish to appear to minimize the importance of the burden of parturition in women with heart disease. It may be the determining factor. Little space is devoted to it here for two reasons.

1. Relatively little quantitative information is available.

2. To bring women with heart disease through pregnancy and up to term in good order and free of cardiac congestion is the chief contribution the physician can make to the delivery.

Skillfully organized and executed delivery is a vital matter to these patients, and here, while continued close cooperation is essential, the obstetrician plays the decisive role. The decreasing cardiac output and blood volume of the final weeks of pregnancy tend to provide the patient with a growing margin of reserve which usually suffices to meet the demands of labor. Unless there are obstetrical indications, cesarean section is not recommended for patients with heart disease.

In drawing toward the close of these two lectures, I shall cite an example

of a patient who illustrates some of the influences which affect the course of heart disease in pregnant women, and some of the principles which underlie the management of such heart disease. This patient is Mrs. D. H., now 31 years of age. Her history is outlined in Figure 3. She was well until age 12, and before that time we consider that she had a normal range of activity. With this normal range, she could support the minimal requirements of her metabolism and she could increase her activity like any other healthy child. At age 12 she had acute rheumatic fever and was hospitalized for six months. At the end of that period the murmur of mitral stenosis was identified. A second, but less prolonged, attack occurred two years later. She had no symptoms of heart disease and no consciousness of limitation throughout childhood and adolescence, but it is fair to assume that the total of her cardiac potential had been reduced.

She married at age 22. At age 23 she was seen at the Lying-in Hospital during her first pregnancy. She did well until the seventh month of that pregnancy when she developed an upper respiratory infection followed by rales at her lung bases. This is interpreted as indicating that the basal cardiac output, plus the output required by her activity, plus the output required by pregnancy, plus the changes produced by the acute respiratory infection, led to a total burden which exceeded the capacity of her heart, and she developed congestive phenomena. On restriction of activity and the administration of digitalis these congestive signs disappeared and she completed her pregnancy without further event.

Her second pregnancy two years later ran an almost identical course. Again

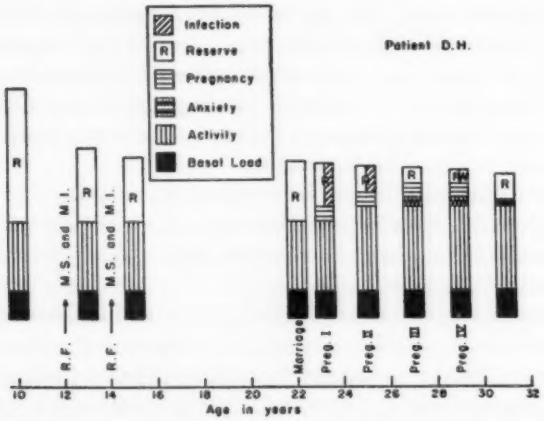

FIG. 3. Cardiac burdens during successive pregnancies in a woman with mitral stenosis. The amount of work the heart is able to do is represented by the total height of the column. The magnitude of the various burdens is represented by the height of the various blocks.

she had an acute respiratory infection at the time of maximum load in the seventh month, and again she developed rales at the lung bases. On this occasion her treatment was by sodium restriction alone. This was as successful as the treatment with digitalis and limitation of activity had been before, the congestion disappeared and the pregnancy went forward. The product of this pregnancy, however, was a boy with severe congenital heart disease, and this provided a sense of anxiety and guilt which added a further burden to all of her subsequent life.

In spite of this added and continuing burden of anxiety, in her third pregnancy she did not develop congestive phenomena at any time. Perhaps this was due to the fact that salt was restricted from the beginning.

Her fourth pregnancy progressed uneventfully to the seventh month or about the period of maximum load. On one Wednesday morning her weekly check-up showed clear lungs and a heart rate of 90. On the same afternoon she had to stand helplessly on a veranda and watch while her son with congenital heart disease was bitten in the face by a bulldog. Within an hour she was in frank pulmonary edema with a pulse rate of 120. Reassurance, a little phenobarbital, and the sight of her son, who wasn't as badly hurt as she feared, was followed by a disappearance of the congestive phenomena. The pulmonary edema was gone within two hours, and the pregnancy progressed uneventfully to term. She is now not pregnant and when recently seen was found to be carrying her basal burden, the burden of household activity, and the persisting burden of anxiety without congestive phenomena or much sense of limitation.

The principle this lecture emphasizes is this: the total burden is the decisive factor. The final Figure 4 relates this concept to an old adage. It has been said already that it is necessary to restrict the total burden of the heart within its individual competence and that sometimes the addition or removal of a small additional burden may make the difference between comfort and disability. The old adage is, "It is the last straw that breaks the camel's back".

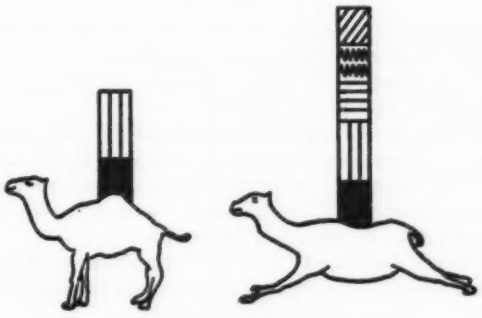

FIG. 4. The last straw.

SUMMARY

The experience here reported indicates that knowledge of the physiological adjustments to pregnancy and the systematic observation of pregnant women with heart disease can be combined usefully and simply to the management of heart disease in pregnant women. The obstetrician and his medical colleagues can integrate the physiology of pregnancy and the physiology of disease so that the course to follow in a given situation is usually clear. When these overall principles are followed the results in terms of maternal health are good. To this extent the original thesis of these lectures is substantiated; knowledge of the circulatory adjustments to pregnancy is useful in the treatment of disease.

Finally, the same principles that have been found useful in the management of pregnant women with heart disease can be applied with directness and success to the management of heart disease in non-pregnant individuals. We can learn from our pregnant cardiacs useful lessons for the care of non-pregnant cardiacs. We can learn, for example, to think about disease and the progress of disease in terms not of single causes, but of superimposed multiple causes, and we can realize the enormous capacity of the organism to adjust itself to disease and the great success that may attend relatively minor adjustments made in the way of therapy by the physician. Many of these successful methods of therapy are quite non-specific—that is, they do not affect any disease process within the heart; they simply modify some of the factors which precipitate symptoms or disabilities.

This experienced organism of ours has many techniques of adjustment to injury and strain. On the whole, these are more effective than the techniques medicine has developed in its long history of devoted effort. Part of our job is to give this built-in tendency to recover a fair chance by removing those terminal straws that may put the final breaking strain on these elegant mechanisms.

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THE INFLUENCE OF HEPARIN ON THE CORTISONE NEPHROPATHY OF THE RABBIT[1]

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Rich, Berthrong and Bennett (1) have reported a renal lesion in rabbits which had been given 7.5 mgms. of cortisone daily for two or three weeks. This lesion consists of a nodular deposit of eosinophilic material in the kidney glomeruli. The deposit was found by Rich to take up the periodic acid-Schiff stain, and he and his collaborators suggested the possible analogy of this lesion to the focal hyaline masses in the glomerular tufts of human diabetics.

In the course of investigating factors in the pathogenesis of the retinopathy of diabetes we have regarded the above type of lesion as an index of effectiveness of our various experimental procedures (2). We have found that the incidence of the renal lesion in the rabbit may be increased to almost 100 per cent if the animals are placed on a diet which is not supplemented by either vitamin B_{12} or aureomycin, and that 80 per cent of alloxan-diabetic rabbits get renal lesions when given 7.5 mgms. of cortisone acetate intramuscularly daily for three weeks. ACTH fails to bring out the lesion in normal rabbits, but in alloxanized rabbits the lesion appears in 70 per cent of animals. We have from time to time noted, and Becker (3) has reported that these renal lesions are occasionally associated with capillary aneurysms in the retina. This latter finding has not been consistent, and in more recent series where we studied additional material prepared by supravital intravascular India ink injection, we have not been able to demonstrate any retinal capillary aneurysms.

We were attracted by the possibility of influencing the kidney lesion with heparin because heparin and cortisone have a number of properties which are antagonistic. Thus, cortisone produces lipemia, and an elevation of serum cholesterol and lipoprotein (4–6), while heparin lowers the serum levels of these materials (7–8). Heparin is well known for its anticoagulant properties while cortisone enhances the coagulability of the blood (9). Heparin prevents the blood eosinophil drop which cortisone occasions (10). Cortisone enhances, and heparin suppresses both the local and general manifestations of the Schwartzman phenomenon (11–12).

[1] This work was supported by a grant from the National Institutes of Health, Division of Neurological Diseases and Blindness.

TABLE I

The Influence of Heparin on the Kidney Lesions in the Rabbit Caused by Cortisone

Group	Cortisone per Day	Heparin per Day, Two Divided Doses	Incidence of Kidney Lesion	Incidence of Clotting Time Increase	Incidence of Lipemia
1.	7.5 mgms.	0	10/12 = 83.3%	0	9/12 = 75%
2.	7.5	50 mgms.	0/18 = 0.00%	16/18 = 88.8%	2/18 = 11.1%
3.	7.5	25	2/18 = 11.1%	4/12 = 33.3%	3/12 = 25.0%
4.	7.5	12.5	8/12 = 66.6%	0/12 = 0.00%	9/12 = 75.0%

EXPERIMENT

Sixty albino male rabbits, each weighing 2000 to 2500 grams, were placed on Sherwood rabbit pellets which were unsupplemented by either aureomycin or vitamin B_{12}. Food and water were provided ad libitum. One week later all rabbits were started on 7.5 mgms. of cortisone acetate in aqueous suspension[2] by intramuscular injection. All rabbits except 12 controls were also given subcutaneous Depo-heparin®[3] in doses ranging from 6.25 to 25.0 mgms. twice daily. Clotting time of venous blood was determined twice weekly by the capillary tube method. This regime was kept up for 21 days, when the animals were killed by pentobarbital overdosage, and the kidneys and eyes removed for pathological examination.

RESULTS

Table I summarizes the results in terms of the influence of heparin on the incidence of glomerular lesions, lipemia and blood clotting time. It will be clear that at all dose levels heparin reduced the incidence of glomerular involvement. The severity of the lesions was also diminished, but less impressively. We also found that inhibition of lipemia and prolongation of blood clotting time were inconstant but associated effects. At the 6.25 mgm. dose level of heparin the incidence of the lesions was somewhat depressed, but blood effects were not in evidence. At all heparin dosages we found, in some instances, a faintly basophilic amorphous material inside Bowman's capsule, in blood vessels, and in collecting tubules. Since a similar deposition was found when we employed heparin alone, it appears that this material is unrelated to the cortisone-induced lesion. Hausman and Dreyfus (13) have detected similar intracapillary precipitates in rabbits given polyanethol sulfonate, a high molecular weight anticoagulant related to heparin.

DISCUSSION

The inhibition of cortisone-induced nephropathy by use of heparin is of interest. Heparin has also been found by Thomas and Good (11) to inhibit

[2] The authors are indebted to Merck & Co., Inc., Rahway, N. J. for this material.

[3] The authors are indebted to The Upjohn Co., Kalamazoo, Mich. for this material.

the renal manifestations of the generalized Schwartzman phenomenon, and by Kleinerman (14) to suppress the experimental nephropathy produced in rabbits by anti-rabbit kidney duck serum. Cortisone has been observed to accentuate the generalized Schwartzman reaction, and Seegal and Hasson (15) have indicated that cortisone may increase the severity of the "nephrotoxic nephritis" produced in the rat by specific anti-kidney serum. Some common mechanism may perhaps be involved in the pathogenesis of these three seemingly diverse lesions.

SUMMARY

The cortisone nephropathy of the rabbit can be suppressed by administration of heparin.

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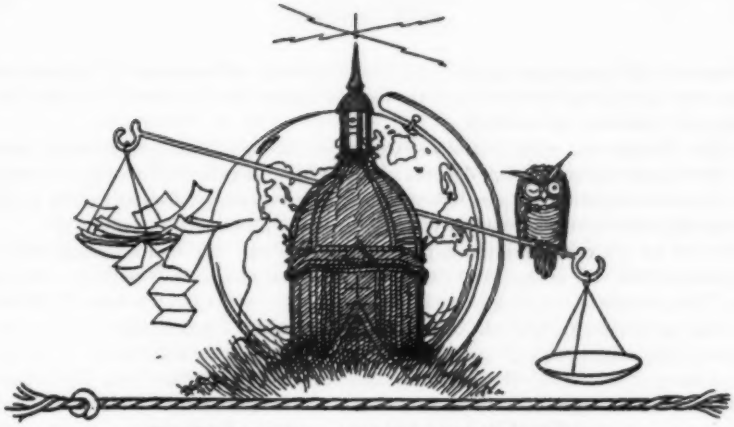

BOOK REVIEWS

(These reviews represent the individual opinions of the reviewers and not necessarily those of members of the Editorial Board of this Bulletin)

Rudolf Virchow: Doctor, Statesman, Anthropologist. By ERWIN H. ACKERKNECHT. 304 pp., $5.00. The University of Wisconsin Press, Madison, Wisconsin.

Rudolf Virchow graduated from medical school in 1843. In a few years he had established himself as the foremost German medical scientist and pathologist. His contributions to our knowledge of thrombosis, embolism, leukemia, inflammation, carcinoma, and cellular physiology are enormous. For almost sixty years he was one of the dominant figures in medicine. At the same time he was active in internal German politics and was important enough in this field to have been challenged to a duel by Bismark. The political turmoil in Germany at that time is an interesting sidelight in this book. Virchow became interested in public health and anthropology and contributed many papers on these subjects. Dr. Ackerknecht has portrayed Virchow as a brilliant pathologist, medical investigator, and dynamic personality. Virchow's biography becomes a history of medicine in the latter half of the nineteenth century because Dr. Ackerknecht portrays Virchow through his works and innumerable papers.

I am amazed to realize how very little medical knowledge existed in 1840 and how far along the road to our present day concepts medicine had advanced by the turn of the century. For this reason Dr. Ackerknecht's biography of Virchow is highly recommended to all.

STANTON L. EVERSOLE

Diseases of the Retina, 2nd edition. By HERMAN ELWYN. 713 pp., $12.00. The Blakiston Co., New York, N. Y.

The second edition of this book on diseases of the retina should be well received. It is in no sense an atlas of fundus conditions, although the twenty color drawings of fundus abnormalities and the numerous black and white illustrations are most helpful in demonstrating typical ophthalmoscopic findings. Rather, it is a comprehensive study which brings together considerable material about all of the usual and many of the rare abnormalities of the retina. Historical data are mentioned briefly when significant. Considerable attention

is directed to the pathologic physiology of these diseases with mention of the systemic as well as the ophthalmic features. And the clinical courses are described in detail. Current concepts of treatment are outlined.

Retinal diseases are systematically discussed under eight headings: diseases resulting from disturbances in circulation; diseases resulting from vascular malformations; degenerative diseases on a hereditary basis; inflammatory diseases; tumors; diseases leading to retinal detachment; developmental anomalies; and radiation injuries.

Some of the material discussed is controversial and one may find occasional points of disagreement with the author. The description of cytoid bodies as "swellings of the nerve fibers," for example, is not in agreement with the concept outlined in the *Atlas of Ophthalmic Pathology* by Friedenwald, et al. The author does mention Friedenwald's concept briefly. In general, the author has kept remarkably up-to-date despite the rapidly advancing knowledge of many of the retinal diseases. A few exceptions may be pointed out. The section on sarcoidosis, for example, fails to make mention of the pre-retinal nodules described by Landers which are considered by many to be an important diagnostic sign. The section on toxoplasmosis lists Wilder's important contribution in the bibliography but not in the text. Internists will take exception to the section on subacute bacterial endocarditis where the author states that the condition "ends fatally in from 4 to 18 months. . . .". The use of antibiotics has altered radically the outcome of this disease. These points are small ones and do not detract from the over-all value of the volume.

The ophthalmologist will find this book particularly valuable as a convenient source of information (with detailed bibliography) on the less frequently encountered retinal diseases. The internist will find this book useful as a reference for the ophthalmoscopic manifestations of systemic disease, but will find it no substitute for the only satisfactory way to learn ophthalmoscopy—namely, the routine examination of every fundus with dilated pupils in a darkened room.

C. T.

Alfred Hospital Clinical Reports, Vol. 3. Edited by R. S. LAWSON and Committee. 115 pp. Printed in Melbourne, Australia by Brown, Prior, Anderson Pty. Ltd.

Volume 3 (1953) of the Clinical Reports published by the Alfred Hospital of Melbourne, Australia, contains several interesting reports by members of its staff on such varied topics as the treatment of head injuries, peptic ulcer, menopause, arthritis and others. Of particular interest to the reviewer was a report by Robert Officer on his experience with carcinoma of the rectum. Apparently he does not believe in the regulation of colostomy function as it is commonly carried out in the United States. Dr. J. M. Buchanan contributed an interesting article on the indications for and technique of vaginal hysterectomy.

EDWARD S. STAFFORD

Cornell Conferences on Therapy, Vol. VI. Edited by HARRY GOLD. 287 pp., $4.00. The Macmillan Co., New York, N. Y.

In this volume are reported fifteen conferences held under the auspices of the departments of medicine and pharmacology of the Cornell University Medical College. The list of subjects discussed consists of the following: treatment of the patient in coma, some therapeutic applications of vasodilating agents, the place of anticoagulants in coronary thrombosis, drugs and radiation in the treatment of leukemia, therapeutic applications of psychosurgery, therapeutic use of combinations of antibiotic agents, one-dose prophylaxis and three-day cure of gonorrhea, ion-exchange resins, treatment of burns, current developments in the treatment of bacterial endocarditis, treatment of osteoporosis, drugs in the

diagnosis of pheochromocytoma, treatment of hiatus hernia, the medical treatment of peptic ulcer and the re-evaluation of the problems of treatment in barbiturate poisoning.

Although these conferences are no substitute for a formal lecture or text-book, they are quite informative and provide material of theoretic and practical interest. Dr. Irving S. Wright's discussion of the use of anticoagulants in coronary thrombosis is particularly of value.

It would help the reader if, in the editing of these conferences, pertinent information were provided for questions left unanswered during the open discussions.

PHILIP F. WAGLEY

Atlas of Exfoliative Cytology. By GEORGE N. PAPANICOLAOU. 56 pp., collection of colored plates by Hashime Murayama. (Looseleaf) $18.00. Published for The Commonwealth Fund by Harvard University Press, Cambridge, Mass.

Tissue cells, shed from epithelial or serosal surfaces, when they have been smeared on a slide and stained have some value in the diagnosis of neoplasms. Dr. George Papanicolaou has been for years the leading exponent of this procedure. His *Atlas of Exfoliative Cytology* is a summary of methods of collecting various human secreta, excreta, exudates, and transudates and how cells in such material can be concentrated and stained. Numerous coloured drawings and discussions of various exfoliated cells compose the body of the work. In addition, the author summarizes his various criteria for malignant cells. The coloured drawings are good and beautifully reproduced. The text is concise and to the point. It would seem this atlas would be the bible for those using the Papanicolaou techniques. However photomicrographs probably would have been of more value than drawings. Just why one would study exfoliated cells to diagnose cancer of the uterine cervix when a biopsy is readily obtainable is not clear. It seems apparent that a biopsy of a tumor is of more diagnostic value than innumerable slides of sloughed-off cells. It is unfortunate that the enthusiasts of exfoliative cytology have misrepresented this to our clinical brethren. When a tumor is inaccessible for biopsy the procedures described here may be of value.

STANTON L. EVERSOLE

The Allergic Child. By HARRY SWARTZ. 297 pp., $3.95. Coward-McCann, Inc., New York, N. Y.

This volume is directed toward the parents of allergic and potentially allergic children. The introductory chapters are concerned with an explanation of somatic and psychological development in reference to the onset of allergy. There is also an excellent summation in laymen's terms of what allergy is thought to be and an explanation of misconceptions in regard to the allergic state. All the various allergic manifestations are described in understandable terms. The technique and variations of treatment are discussed and evaluated. There is an interesting glossary which will serve well the physician who must treat allergic diseases. He should be familiar with all of the potential sources of hypersensitivity. The list of food preparations, which are especially prepared for allergic individuals, is excellent and for the patient, who is truly allergic to foods, this list should be helpful.

LESLIE N. GAY

Acute Anuria. A Study Based on Renal Function Tests and Aspiration Biopsy of the Kidney. By CLAUS BRUN. 215 pp., Dan. kr. 30.00. Ejnar Munksgaard, Copenhagen, Denmark.

The author states that his main concern lies with "ischaemic anuria or acute anuric renal failure" which is accompanied by histologic changes in the renal tubules and inter-

stitial tissue characteristic of "acute tubulo-interstitial nephritis"—a circumstance similar to that which Lucké popularized as "lower nephron nephrosis".

The first portion of the text contains a concise review of the history and important literature briefly describing the nature of the syndrome from the viewpoints of the pathologist, physiologist and clinician. A second portion details the experiences derived from observing 32 patients with acute renal failure, 13 of whom presented themselves in a state of shock and 10 of whom had received sulfonamides prior to the onset of oliguria. The clinical course of these individuals is outlined and their therapeutic regimens presented. Renal function tests (clearance of urea, creatinine, inulin, and p-amino-hippuric acid) were performed on nearly half of the patients and indicated that "impairment of glomerular and tubular function persisted long after the urine flow had become normal" though within 6–12 months all values had returned to the range usually observed. Finally, the histologic changes in kidney tissue obtained through per-cutaneous aspiration biopsy and at autopsy are described and compared. The interstitial edema and cellular infiltration as well as the ubiquity of the tubular lesions is emphasized and renal ischemia is implicated as the important common pathogenetic factor.

This thesis, I think, contains no startlingly new facts. It is difficult to draw conclusions as to the true nature of altered renal function based on our present methods of investigation. The lack of correlation between "functional disturbance" and "histologic disturbance" in this particular instance poses more of a challenge than a surprise.

However, Dr. Brun's presentation is comprehensive, intelligible, judiciously illustrated and documented by a well selected bibliography. It affords worthwhile reading for the student, clinician and renal physiologist.

A. H. O., Jr.

Manual of Clinical Mycology, 2nd edition. By Norman F. Conant, David T. Smith, Roger D. Baker, Jasper L. Callaway and Donald S. Martin. 456 pp., $6.50. W. B. Saunders Co., Philadelphia, Pa.

In these days, when the management of serious bacterial infections is much less of a problem than formerly, we are aware of at least a relative increase in the incidence of diseases due to fungi. It is timely, therefore, to have an up-to-date textbook on this subject by a group of workers who are recognized authorities in this field. There are short, concise descriptions of the various fungi and the diseases they produce, with inclusion also of brief statements regarding pathological findings and the most effective therapy. An added feature of real value is the inclusion of a well-chosen bibliography after each chapter.

The chapter on blastomycosis, summarizing the relatively extensive experience at their clinic, with this rare and serious infection, is of particular interest, as are those on coccidioidomycosis and histoplasmosis. The several rather striking similarities in disease patterns of these latter two conditions is shown quite clearly. The text is well illustrated by numerous reproductions of cultures, microscopic preparations and X-rays. There is a separate section at the end giving cultural methods and formulas for the preparation of media, which should help make this an excellent reference book for anyone engaged in clinical mycology.

A. Murray Fisher

Atlas of Orthopedic Traction Procedures. By Carlo Scuderi. 230 pp., $12.50. The C. V. Mosby Co., St. Louis, Missouri.

This could be a very useful book in the libraries of hospitals where there is a lack of a well-trained orthopedic staff. It contains many clear photographic pictures and lucid de-

scriptions of various types of traction. Such a publication can occasionally reduce the time required for gathering pertinent information about traction therapy. The book could be improved by including pictures of x-rays demonstrating the results of traction.

W. RICHARD FERGUSON

Atlas of Operative Technic—Anus, Rectum and Colon. By HARRY E. BACON AND STUART T. ROSS. 301 pp., $13.50. The C. V. Mosby Co., St. Louis, Missouri.

Dr. W. Wayne Babcock introduces this atlas with the remark, "The members of a group who have been watching an operative clinic will often leave with widely divergent impressions as to what was seen (or was not seen)." Certainly this observation is in itself indicative of Dr. Babcock's acute understanding of one of the difficulties inherent in surgical teaching. To quote him further: "One sees only what he mentally understands."

If an atlas is to bridge the gap between sight and understanding, it must, of necessity, fulfil certain prerequisites. It must, of course, be accurate. It must be lucid from the standpoint of artistic technique without being overly diagrammatic. Above all it must manifest a harmony of purpose on the part of the author and artist which will further the mental understanding of which Dr. Babcock speaks.

This volume is divided into two basic parts, the first dealing with anorectal operations and the second with colonic operations. Illustrations are by Melford D. Diedrick, University of Buffalo; William B. McNett, Temple University; and Leon Schlossberg of Johns Hopkins University. The format is that of drawings on the odd numbered pages, faced by a commentary which includes preliminaries, preparation, position, anaesthesia, technique (in numbered sequence) and remarks on post-operative patient care.

The accuracy of the drawings and text, as well as the lucidity of presentation are of the highest order. It is not mere prejudice which causes us to single out Mr. Schlossberg for special mention. In the company of other, and obviously able artists, his work is a shining example of outstanding skill and talent.

If we are to criticize without carping we would take issue with the authors on the point of whether or not their textual material really contributes to the understanding of which we spoke above. The first 69 pages of this atlas are devoted to so-called general considerations which begin with surgical anatomy and cover anesthesia, incisions, and preoperative and postoperative care. Appropriately, the discussions of patient care are limited as is proper in an atlas. However, this curtailed discussion contributes little, gives an impression of over-simplification, and is, therefore, distracting. These same criticisms are to be leveled at the discussions accompanying the operative description. With regard to the description of incisions, the techniques are, or should be, familiar to surgeons, and discussions and illustrations might, in our opinion, better be limited to new or original thoughts on the subject. The discussions of surgical anatomy are appropriate but misplaced. We should have preferred each as an introduction to its respective part of the book, to serve as an orientation to the philosophy of what is demanded in the particular surgical techniques. With these alterations, which are not profound, we feel that there would be clearer direction for the reader, enabling him to understand what he would see, and permitting him to insert the operation into its proper context of continuous medical care, on the basis of his own facilities, ability and experience. Nevertheless, it must be stated that this volume of operative technique is less guilty of containing material not immediately to the point than most we have seen, and is superior in every way.

It is appreciated that all procedures for all conditions are not to be expected. We could comment, however, upon several of the techniques. In the experience of most the technique described for dealing with congenital arrest in descent of the rectum is not completely

satisfactory. It has been necessary to divide the perineum more widely to permit the meticulous dissection necessary. The text makes no mention of a criterion by which one decides when to explore such patients abdominally.

No recognition is made of the technique for hemorrhoidectomy expounded by Dr. Harvey Stone and used so widely. Nor is there mention of the Wreden-Stone fascial sling procedure for incontinence. These are significant omissions.

We do not propose to enter into polemics regarding the operation for pilonidal sinuses, but we fail to recognize its place in this atlas (as we fail to recognize its position in Dr. Bacon's text-book).

The section on colonic surgery is beautifully done.

It is undeniable that Dr. Bacon and Dr. Ross have contributed a work which is valuable, artistic, and destined to occupy a conspicuous position on the shelves of surgical libraries. We feel that the minor criticisms which we have made represent the slight irregularities of a first edition and do not in any way seriously detract. The volume is a splendid complement to the treatise of Dr. Bacon on the lower bowel and together they represent an attractive, understandable and definitive work.

JACOB C. HANDELSMAN

Toxicity of Industrial Organic Solvents. By ETHEL BROWNING. 411 pp., $8.00. Chemical Publishing Co. Inc., New York, N. Y.

In 1935, the Medical Research Council of Great Britain asked Dr. Ethel Browning to compile a summary of the available information on the common industrial solvents. Dr. Browning's review of the literature, one of the earliest publications on the organic solvents, appeared in 1937 as Report No. 80 in the Council's Series of Industrial Health Research Board Reports. Because of the large amount of new information on this subject, Dr. Browning revised this publication to include the literature up to 1948. This second edition of the report was published in Great Britain in 1952 and reprinted in book form in the United States in 1953.

Dr. Browning's review gives a summary of the important toxicological data on 126 of the more common solvents. The solvents are grouped according to their chemical structure under the following chapter headings:—hydrocarbons, chlorinated hydrocarbons, alcohols, ethers, esters, ketones, glycols, amines and coal tar bases, nitrocompounds, and miscellaneous compounds. This arrangement of the data allows comparison of closely related compounds. For each solvent, Dr. Browning gives the properties, uses, general toxicity and permissible concentrations, toxic effects on animals, and toxic effects on man. Under the toxicity sections, the acute and chronic effects are discussed separately and, where the data are extensive, the material is grouped under further subheadings. In addition, the manufacturing processes, the procedures for estimating the concentration of the solvent in the air and in biological material, and the methods of treatment are included in the discussions of the more important solvents.

In general, the space devoted to each solvent is short, being three pages or less for 80 per cent of the solvents. However, longer reviews are given of benzene (43 pages), carbontetrachloride (21 pages), methyl alcohol, benzine, trichlorethylene, and carbon disulphide (12–14 pages each).

The data are well organized and thoroughly documented. The extensive bibliographies at the ends of the chapters cover the literature of many countries and thus serve as excellent sources for further reference. The phraseology is not stereotyped, as is often the case in such reviews of literature; the presentation is interesting, clear, and concise. The detailed

table of contents and the index make information on these solvents easily and quickly available.

ANNA M. BAETJER

Fundamentals of Otolaryngology, 2nd edition. By LAWRENCE R. BOIES. 487 pp., $7.00. W. B. Saunders Co., Philadelphia, Pa.

This is the second edition of a very well known text-book following the first edition by four and one half years. It is pleasant to read and has many illustrations of practical value.

In reviewing this book, it is important to keep in mind the intentions of the author and how he accomplished his objectives. This is intended specifically for the undergraduate medical student and for the physician who is not a specialist in otolaryngology. This volume is full of fundamentals of otolaryngology in all its phases but not in such a detailed form that they are difficult to comprehend. It is not intended as a complete reference text-book. With this in mind, the author should be complimented for a fine achievement. There is a need for such books in order to teach the fundamentals to doctors who have no intention of going into this specialization. This book is of great value to the general physician and to the medical student.

There are thirty-three chapters in this edition and each one covers a specific otolaryngologic subject with emphases on the basic fundamentals. The author has written a special introduction to the book entitled, "Introduction to Modern Otolaryngology" which is an interesting verbal description of the recent changes in the specialty of Otolaryngology and also just what might be expected in the future. It is worth reading. The last chapter of the book is titled, "Modern Medication in Otolaryngology" and this is a chapter devoted to specific therapeutic measures and to the recent changes in therapeutic measures. There are listed many prescriptions and detailed therapy of great value.

This is a well organized work and highly recommended for teaching purposes and for a handy general reference book.

A. P. W.

Der Herzkatheterismus bei Angeborenen und Erworbenen Herzfehlern. (Heart Catheterization in Congenital and Acquired Heart Disease). By O. BAYER, FR. LOOGEN AND H. H. WOLTER. 191 pp., $8.60. Georg Thieme Verlag, Stuttgart, Germany. Sold by Intercontinental Medical Book Corporation, New York, N. Y.

This monograph, which is based on 800 cardiac catheterizations during the past five years, is dedicated to Dr. V. Forssman, the German physiologist who in 1928 performed the first 8 such procedures upon himself.

Technic and methods used are discussed in great detail and are, in general, the same as those used in the United States. Much emphasis is placed on the tracings of intracardiac and intravascular pressures in relation to the physiological events, especially upon the pulmonary "capillary" pressure and its diagnostic value. Besides the usual calculations of the Fick principle by analysis of expired air and blood gases, methods are described and calculations given of circulatory and pulmonary resistance, estimations of the orifice of the mitral, pulmonary and tricuspid valves, and of the heart energy expenditure for right and left ventricles.

The second part of the book gives an excellent review of congenital heart disease. Good descriptions of the morphological picture, physiological findings, and clinical appearance of many malformations are given with good reproductions of pressures, phonocardiograms, EKG tracings and X-rays.

The last part covers descriptions and figures of acquired heart disease and includes good studies of 10 patients with mitral stenosis before and after operation. One table shows estimates of mitral valve orifice area in relation to body surface area.

This is a remarkably comprehensive work on the physiological, morphological and clinical aspects of cardiac diagnosis, and was written with knowledge and appreciation of the international literature in this field.

EVA BOECKH

Alcoholism. By JACKSON A. SMITH. 72 pp., $3.00. J. B. Lippincott Co., Philadelphia, Pa.

This book is a very concise and understandable discussion of the common problems encountered in treating alcoholic patients. The material was initially published in *American Practitioner and Digest of Treatment* and seems to be intended for general practitioners. Controversial material and theoretical discussion are minimized. The author presents the problems of this very unhappy group of patients in terms of what can be done most directly and effectively. He deals with the behavior patterns of alcoholic patients, the use of psychotherapy with chronic alcoholics, the use of antabuse, treatment of delirium tremens, some other techniques in treating alcoholics, and a summary of treatment for the general practitioner. He stresses appropriately the difficulties one encounters in using psychotherapy and in carrying out chemical treatment. The need for the patient's cooperation and the difficulty of obtaining it are emphasized repeatedly.

This volume can be recommended for the non-psychiatric reader who is interested in acquiring information about the alcoholic patient and ways of helping him. As an example of what is not considered in the book, there is the question of developing community services which will first help the alcoholic patient acknowledge his problem and then provide the aid he needs.

JEROME STYRT

Fluid and Electrolyte Therapy. By FRANKLIN L. ASHLEY AND HORACE G. LOVE. 72 pp., $3.00. J. B. Lippincott Co., Philadelphia, Pa.

This new monograph has no features which make it an obvious improvement over the existing literature in its field. Its purpose, to present some fundamental principles, is not met since it is marred by errors, by omissions, and by loose descriptions of bodily adjustments to loss of water and of electrolytes.

K. L. ZIERLER

The Billroth I Gastric Resection. With Particular Reference to the Surgery of Peptic Ulcer. By HORACE G. MOORE, JR., AND HENRY N. HARKINS. With a Foreword by DR. GOSTA BOHMANSSON and a Preface by Dr. JOHN M. WAUGH. 175 pp., $7.50. Little, Brown & Co., Boston, Mass.

This account of the origin and development of the Billroth I operation is well done. This commendation is particularly applicable to the historical data which have been assembled with painstaking precision. It is encouraging to find credit given in proper proportion to all of the surgeons who had a part in the origin, the growth and the modifications of this operation. The authors make a very earnest attempt to point out the limitations as well as the virtues of this particular procedure by quoting freely from the writings of those who have had the greatest experience with it. One might like to see more comparisons made between the Billroth I and the Polya operations, rather than with the Billroth II. The greatest limitation of this book is one which is inherent in any statistical evaluation of a subject in which the intangible and immeasurable quantity called "surgical judgment" plays so

large a role. An inexperienced person reading the section on the technique of the operation might be led to attempt it on occasions when a more experienced surgeon would shun it. This is just another way of saying that one cannot learn surgery out of a book, but that one can learn *about* surgery by reading. The present volume is an instructive and helpful one for everyone who is anxious to increase his knowledge about gastric surgery.

W. M. F.

BOOKS RECEIVED FOR REVIEW

A.M.A. Fundamentals of Anesthesia, 3rd edition, 279 pp., $6.00. W. B. Saunders Co., Philadelphia, Pa.

Antibiotika-Fibel. Indikation und Anwendung der Chemotherapeutika und Antibiotika. By ALBERT M. WALTER AND LUDWIG HEILMEYER. 813 pp., Ganzleinen DM 79 ($18.80). Georg Thieme Verlag, Stuttgart, Germany.

Chemotherapy of Infections. By H. O. J. COLLIER with a Foreword by SIR ALEXANDER FLEMING. 248 pp., $4.00. John Wiley & Sons, New York, N. Y.

Ergebnisse der Gesamten Tuberkuloseferschung, Bd. 12. By H. BEITZKE, ST. ENGEL, L. HEILMEYER, J. HEIN AND E. UEHLINGER. 488 pp., Ganzleinen DM 65. Georg Thieme Verlag, Stuttgart, Germany.

Glandular Physiology and Therapy—A Symposium, 5th edition. Prepared Under the Auspices of the Council on Pharmacy and Chemistry of the American Medical Association. 611 pp., $10.00. J. B. Lippincott Co., Philadelphia, Pa.

Handbook of Tropical Dermatology and Medical Mycology, Vol. II. Edited by R. D. G. Ph. Simons. 854 pp., with an appendix of 15 pp., $15.00. The Elsevier Press, Houston, Texas.

Man Above Humanity. A History of Psychotherapy. By WALTER BROMBERG. 342 pp., $5.75. J. B. Lippincott Co., Philadelphia, Pa.

Metabolic Integrations. By P. G. WATSON. 15 pp., 4s. net. W. Heffer & Sons Ltd. Cambridge, England.

A Methodological Psychiatric and Statistical Study of a Large Swedish Rural Population. By TAGE LARSSON AND TORSTEN SJÖGREN. 250 pp., 25 Swedish Crowns. Ejnar Munksgaard, Copenhagen, Sweden.

New and Nonofficial Remedies. Accepted by the Council on Pharmacy and Chemistry, American Medical Association for 1954. 607 pp., $2.65. J. B. Lippincott Co., Philadelphia, Pa.

Physiology and Biochemistry of the Skin. By STEPHEN ROTHMAN. With Contributions by ZACHARY FELSHER, PETER FLESCH, A. BUNSEN LERNER, ALLAN LORINCZ, HERMANN PINKUS AND GEORGE C. WELLS. 741 pp., $19.50. The University of Chicago Press, Chicago, Illinois.

Practical Fluid Therapy in Pediatrics. By FONTAINE S. HILL. 275 pp., $6.00. W. B. Saunders Co., Philadelphia, Pa.

A Primer of Pulmonary Function. By HAROLD GUYON TRIMBLE AND JAMES KIERNAN. 22 pp. Printed through the cooperation of The California Tuberculosis and Health Association.

William H. Welch and the Rise of Modern Medicine. By DONALD FLEMING. 216 pp., $3.00. Little, Brown & Co., Boston, Mass.

Why We Became Doctors. Edited by NOAH D. FABRICANT. 182 pp., $3.75. Grune & Stratton, New York, N. Y.

Corrections

Volume 95, Number 2, August 1954

Page 95: "Figure 8 A and B" should read "Figure 9 A and B". "Figure 9" should read "Figure 8".

Pages 96 and 101: The plates labeled FIG. 10 D and FIG. 19 should be interchanged.

Page 97: "10D" should read "10E." "Figure 10E" should read "Figure 10D."

Page 109: "Fig 20 C" should read "Fig. 20 B."

9"

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D."